

US EPA ARCHIVE DOCUMENT

Shaughnessy No.: 101101
Date Out of EFGWB: 9/24/90

To: R.J. Taylor
Product Manager 25
Registration Division

From: Henry P. Nelson, Acting Chief *H. Nelson*
Environmental Chemistry Review Section #3
Environmental Fate and Ground Water Branch/EFED

Through: Henry Jacoby, Chief *Henry Jacoby*
Environmental Fate and Ground Water Branch/EFED

Attached, please find the EFGWB review of . . .

Reg./File # : 352-390
Chemical Name : Metribuzin
Type Product : Herbicide
Product Name : _____
Company Name : DuPont
Purpose : Accumulation in confined rotational crops

Date Received: _____ EFGWB # (s): 90454, 90264-6
Action-Code : _____ 90-0263? 90-0264-67
90-0454

Deferrals to: _____ Ecological Effects Branch, EFED
_____ Science Integration and Policy Staff,
_____ Non-Dietary Exposure Branch, HED
_____ Dietary Exposure Branch, HED
_____ Toxicology Branch I, HED
_____ Toxicology Branch II, HED

1. CHEMICAL: Metribuzin
2. TEST MATERIAL: Not applicable.
3. STUDY/ACTION TYPE: Rotation restriction to peanuts.
4. STUDY IDENTIFICATION: Accumulation in confined rotational crops
5. REVIEWED BY:

A. Abramovitch, Ph.D.
Chemist
EFGWB/EFED/OPP
Review Section #3

Signature: *A. Abramovitch*

Date: SEP 5 1990

6. APPROVED BY:

Henry P. Nelson, Ph.D.
Acting Chief
EFGWB/EFED/OPP
Review Section #3

Signature: *H. P. Nelson*

Date: 9/18/90

7. CONCLUSION:

The registrant has submitted satisfactory storage stability and recovery efficiencies from soil and plant samples rendering the study as acceptable. Therefore, the confined crop rotation to peanuts can be used to establish rotational restriction interval. The study indicated that 0.6 ppm of uncharacterized polar material were found in the peanut foliage which is used as feed. However, an August 13, 1990 memorandum from Stephen Dapson of the Toxicology Branch to Robert Taylor of RD indicated that the Toxicology Branch "does not consider the terminal polar compounds that constitute the major portion of the peanut foliage residues to be toxicologically significant."

8. RECOMMENDATIONS:

EFGWB does not object to a rotational interval to peanuts of 8 months with a maximum application rate of 0.55 lb ai/acre.

9. BACKGROUND:

- A. Introduction EFGWB reviewed in 1988 a confined rotational crop to peanuts study at a level of 1 lb ai/acre which is 1.8x the 0.55 ai/acre application rate. The study was submitted in order to support a reduction

of the crop rotation to peanuts restriction from 12 to 8 months. Based on the review the study was considered supplemental and R. Taylor of RD/OPP informed DuPont in a April 13, 1988 letter to Ms. Chubb (see attached letter) that:

1) a storage stability data are needed to render the study acceptable.

2.) If the missing stability data are found acceptable and DEB does not express a concern on the residues of metribuzin in the foliage, then the study could support a rotational interval reduction to 8 months on peanuts at 0.55 lb ai/acre application rate.

B. Directions for Use A label was not enclosed.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

See attached confined crop rotation study on peanuts review of the study.

11. COMPLETION OF ONE-LINER: Not completed

12. CBI APPENDIX: None



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

REVIEWER

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

13

MEMORANDUM

SUBJECT: DEB deferral in reference to significance of polar compounds in peanut foliage treated with Metribuzin. EPA Identifying Nos.: 352-382 and 352-390, EPA MRID No.: none, EPA Record Nos.: 261388 and 261389, HED Project No. 0-0940, Caswell No. 33D.

TO: Robert Taylor/Vickie Walters (PM 25)
Herbicide-Fungicide Branch
Registration Division (H7505C)

FROM: Stephen C. Dapson, Ph.D. *Stephen C. Dapson* 8/6/90
Pharmacologist, Review Section I
Toxicology Branch-Herbicide, Fungicide, Antimicrobial Support/HED (H7509C)

THRU: Yiannakis M. Ioannou, Ph.D., D.A.B.T. *Y. M. Ioannou* 8/6/90
Section Head, Review Section I

and
Marcia van Gemert, Ph.D. *M. van Gemert* 8/9/90
Chief, Toxicology Branch-Herbicide, Fungicide, Antimicrobial Support
Health Effects Division (H7509C)

Registrant: Mobay Corporation

Action Requested: Review deferral from DEB in reference to significance of polar compounds in peanut foliage treated with Metribuzin.

Recommendations: The Toxicology Branch-Herbicide, Fungicide, Antimicrobial Support does not consider the terminal polar compounds that constitute the major portion of the peanut foliage residues to be toxicologically significant.

The only identified polar metabolite (since the second polar metabolite could not be identified and was apparently unstable) has been found in rat and dog metabolism studies submitted previously in support of the toxicology data requirements; therefore any effect of this metabolite would be covered by the previously submitted and accepted, chronic toxicity studies in the mouse, rat, and dog.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 15 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. Nos. 352-382 and 352-390. Metribuzin.
Rotational Crop Accumulation Study. Deferral from EFGWB.
MRID No. 405777-01. DEB Nos. 5156 and 5157.

FROM: Linda S. Propst, Chemist
Dietary Exposure Branch
Health Effects Division (H7509C)

Linda S. Propst

THRU: Andrew R. Rathman, Section Head
Special Registration Section 1
Dietary Exposure Branch
Health Effects Division (H7509C)

ARR

TO: Robert J. Taylor, PM #25
Fungicide-Herbicide Branch
Registration Division (H7505C)
and
Toxicology Branch
Health Effects Division (H7509C)

E.I. du Pont de Nemours & Co., Inc. has submitted a rotational crop accumulation study for metribuzin in an attempt to reduce the existing 12-month rotation restriction for peanuts to 8 months.

Environmental Fate Ground Water Branch has reviewed this study and concluded (A. Reiter, 12/21/88) that soils residues of radiolabeled metribuzin were not detectable (<0.004 ppm) for the 8 month rotational intervals at exaggerated (1.8X) rates. Likewise, the total ¹⁴C residues were very low (0.06 ppm). The levels in the nut meat and shell were 0.027 ppm and 0.066 ppm, respectively, and would be expected to be even lower if the label (vs. exaggerated) rate were used. However, approximately 0.6 ppm levels of incompletely characterized radiolabeled material were found in the foliage portions of peanuts after an 8 month interval.

Environmental Fate Ground Water Branch has asked Dietary Exposure Branch if peanut foliage is a feed item and if Dietary Exposure Branch can support this 8 month interval because of the residues on foliage.

Conclusions and Recommendations

Dietary Exposure Branch considers peanut foliage a feed item and therefore, in this case, a rotational crop tolerance will be required.

However, if Toxicology Branch does not consider the terminal polar compounds that constitute the major portion of the foliage residues to be toxicologically significant, no tolerance will be required.

cc: Reading File, Circulation, Subject File, Reviewer, Branch
Chief, PMSD/ISB
RDI: A. R. Rathman, 6/14/89; E. Zager, 6/15/89
H7509C:DEB:LSP:lsp:CM-2:Rm803C:557-7324:6/15/89

DATA EVALUATION RECORD

CHEM 101101

Metribuzin

§165-1

FORMULATION--00--ACTIVE INGREDIENT

Naidu, M.V. 1988. Metribuzin confined accumulation study on peanuts. Laboratory Project ID AMR-563-86. Unpublished study prepared and submitted by E.I. du Pont de Nemours and Company, Inc., Wilmington, DE.
MRID 40577701

DIRECT REVIEW TIME = 16

REVIEWED BY: J. Harlin TITLE: Staff Scientist

EDITED BY: K. Patten TITLE: Task Leader

APPROVED BY: W. Spangler TITLE: Project Manager

ORG: Dynamac Corporation
Rockville, MD
TEL: 468-2500

APPROVED BY: A. Reiter *A. Reiter* DATE: December 20, 1988
TITLE: Chemist
ORG: EFGWB/HED/OPP

This study was provided by the registrant as support data for reducing the rotational interval for metribuzin on peanuts from 12 months to 8 months.

CONCLUSIONS:

Confined Accumulation - Rotational Crops

This study provides supplemental information towards the registration of metribuzin. This study does not fulfill EPA Data Requirements for Registering Pesticides because peanuts are not a standard crop. More importantly, it does not support the requested reduction in rotational interval for peanuts because storage stability data were not provided and the residues found in peanut foliage may be of concern.

SUMMARY OF DATA BY REVIEWER:

[¹⁴C]Metribuzin residues accumulated in peanuts (mature foliage, nut shells, and nut meats) that were planted in sandy loam soil 125 and 246 days after 5-[¹⁴C]metribuzin (radiochemical purity >98%) was applied to the soil at 1 lb ai/A (1.8x the maximum application rate). Total [¹⁴C]residues were 1.7-3.3x higher in nut meats, nut shells, and foliage

from the 125-day rotation compared to the 246-day rotation. In both the 125- and 246-day rotations, the majority (>80%) of [¹⁴C]residues were either polar compounds or unextractable; no organosoluble [¹⁴C]residues were present in quantities sufficient to identify.

The concentrations of total [¹⁴C]metribuzin residues in peanuts from the 125-day rotation were: 0.047 ppm in the nut meats; 0.221 ppm in the nut shells; and 1.811 ppm in the foliage. In the nut meats, organosoluble [¹⁴C]residues totaled 0.008 ppm, water-soluble [¹⁴C]residues totaled 0.018 ppm, and unextractable [¹⁴C]residues totaled 0.017 ppm. In the nut shells, organosoluble [¹⁴C]residues totaled 0.012 ppm, water-soluble [¹⁴C]residues totaled 0.081 ppm, and unextractable [¹⁴C]residues totaled 0.097 ppm. In the foliage, organosoluble [¹⁴C]residues totaled 0.034 ppm, water-soluble [¹⁴C]residues totaled 1.580 ppm, and unextractable [¹⁴C]residues totaled 0.158 ppm. The aqueous extract from the foliage contained 14 compounds, two of which were "major". Polar Metabolite I, detected at 0.624 ppm, was tentatively identified as

N-glucoside of 6-tert-butyl-1,2,4-triazin-3,5(2H,4H)-dione;

Polar Metabolite II, detected at 0.521 ppm, was highly unstable and could not be identified. Acid hydrolysis or enzyme hydrolysis with β -glucosidase or cellulase of the extracted crop fractions did not release any significant organosoluble [¹⁴C]residues.

The concentrations of total [¹⁴C]metribuzin residues in peanuts from the 246-day rotation were: 0.027 ppm in the nut meats; 0.066 ppm in the nut shells, and 0.628 ppm in the foliage. In the nut meats, organosoluble [¹⁴C]residues totaled 0.005 ppm, water-soluble [¹⁴C]residues totaled 0.017 ppm, and unextractable [¹⁴C]residues totaled 0.009 ppm. In the nut shells, organosoluble [¹⁴C]residues totaled 0.004 ppm, water-soluble [¹⁴C]residues totaled 0.035 ppm, and unextractable [¹⁴C]residues totaled 0.028 ppm. In the foliage, organosoluble [¹⁴C]residues totaled 0.009 ppm, water-soluble [¹⁴C]residues totaled 0.502 ppm, and unextractable [¹⁴C]residues totaled 0.061 ppm. The aqueous extract from the foliage contained "several" compounds; polar Metabolites I and II were detected at 0.139 and 0.238 ppm, respectively.

In the soil, [¹⁴C]residues were 0.326 ppm immediately posttreatment, 0.181 ppm at 125 days, 0.125 ppm at 246 days, 0.082 ppm at 267 days, and 0.064 ppm at 393 days posttreatment. [¹⁴C]Metribuzin decreased from 0.278 ppm immediately posttreatment to 0.12 ppm at 125 days and <0.004 ppm at 246-393 days. Organosoluble metribuzin [¹⁴C]degradates identified in the soil were:

6-tert-butyl-1,2,4-triazin-3,5(2H,4H)-dione (0.047 ppm);

6-tert-butyl-3(methylthio)-1,2,4-triazin-5(4H)-one (0.014 ppm); and

4-amino-6-tert-butyl-1,2,4-triazin-3,5(2H,4H)-dione (0.005 ppm).

During the 393-day study, organosoluble [^{14}C]residues in the soil decreased from 97.2 to 26.6% of the recovered, water-soluble [^{14}C]residues increased from 1.8 to a maximum 28.6% (246 days), and unextractable [^{14}C]residues increased from 0.9 to 50.0%.

DISCUSSION:

1. The concentration of metribuzin residues in the soil was 0.326 ppm at day 0 for a 14-inch deep segment; this is equivalent to 1.3 lb ai/A and confirms that the stated application rate was achieved and actually reflected a slightly greater rate. The registrant stated that 1 lb ai/A was equivalent to 1.8x the maximum registered application rate.
2. The following items are missing from this study:
 - a. Storage stability data were not provided to confirm that the [^{14}C]-residues in the crops and soil did not degrade between sampling and analysis.
 - b. Recovery efficiencies from soil and plant samples fortified with metribuzin and its degradates were not provided.
 - c. The CEC of the soil was not provided.
2. The registrant stated that Polar Metabolite II may be a polysaccharide conjugate or a mixture of several sugar conjugates, but because a small amount of sample was available and the MS analysis was complex, further analysis could not be carried out.
3. The levels in the nut meat and shell were only 0.027 ppm and 0.066 ppm, respectively, and would be expected to be even lower if the label (vs. exaggerated) rate were used. However, approximately 0.6 ppm levels of incompletely characterized radiolabeled material were found in the foliage portions of peanuts after an 8 month rotational interval. this study does not support the requested reduction from 12 months.
4. Soil residues of radiolabeled metribuzin were not detectable (<0.004 ppm) for either the 4 or 8 month rotational intervals at exaggerated (1.8X) rates. Likewise, there was no significant difference between the total ^{14}C residues for either interval (0.08 or 0.06 ppm, respectively). These levels would be expected to be below 0.04 ppm at the maximum label rate, and thus support the request for the reduction to an 8 month crop rotation interval for peanuts. Finally, from the increase in total recovered unextracted residues (0.9 to 50%, day 0 to 393) and from the decrease in the organosoluble residues (97 to 27%), it is suggested that the radiolabeled carbon is progressing into the general carbon pool.

MATERIALS AND METHODS

MATERIALS AND METHODS:

Sassafras sandy loam soil (76% sand, 16% silt, 8% clay, 0.7% organic matter, pH 6.5) was used to fill eight pots (15-inch diameter, 14-inch depth), which were then buried at ground level in the field. The soil in each pot was surface-treated with an aqueous solution of 5- ^{14}C metribuzin (radiochemical purity >98%, specific activity of 7.54 Ci/mg, Mobay Chemical Corporation) at 12.8 mg ai/pot (1 lb ai/A). The treated soils were kept in the field for 125 days, and then were transferred into a greenhouse maintained at 27-30°C. Four of the pots were planted to peanuts immediately (125 days); the remaining four were aged in the greenhouse until 246 days posttreatment, at which time the pots were planted to peanuts. During the aging period, the treated soil was kept moist and any weeds that sprouted were pulled and left on top of the soil surface to dry and decompose. During the crop growth period, the plants were watered "as necessary" and a 14-hour photoperiod was maintained (light source unspecified).

The peanuts were harvested at maturity (142-147 days postplanting), which was 267 days posttreatment for the 125-day rotation and 393 days posttreatment for the 246-day rotation. Plant samples were divided into foliage and nuts. All plant tissues were washed with water and air-dried; the nuts were separated into shells and meats; and the foliage, nuts and meats were freeze-dried and frozen (-20°C) until analysis. Soil samples (0- to 14-inch depth) were taken at the times of treatment, planting, and harvest (0, 125, 246, 267, and 393 days posttreatment). Soil samples were air-dried overnight, homogenized, and frozen (-20°C) until analysis.

The plant samples were homogenized, and portions of each sample were analyzed for total radioactivity by LSC following combustion. Additional material was extracted twice with hexane using "gentle refluxing and stirring", then four times with 20% aqueous acetonitrile using refluxing and stirring for one hour each time. The aqueous acetonitrile extracts were combined and concentrated using a rotary evaporator, and the residue was partitioned between water and chloroform. All fractions were analyzed for total radioactivity by LSC. The organosoluble extracts, along with nonradiolabeled reference standards, were analyzed by TLC on silica gel plates developed in benzene:chloroform:dioxane (80:60:60). Areas of radioactivity were visualized by autoradiography; nonradioactive standards were located by fluorescence quenching under UV light. Also, ^{14}C -compounds were detected and quantified using a TLC linear analyzer, and were identified by comparison to ^{14}C metribuzin reference standards and to the R_f of metribuzin. Radioactive zones were scraped from the TLC plates and quantified by LSC as a water gel. Additional organosoluble extracts were analyzed for degradates by reverse-phase HPLC. Unextractable ^{14}C residues remaining in the plant tissues were quantified by LSC following combustion.

Subsamples of the extracted plant fractions or extracts were analyzed by enzyme hydrolysis, acid hydrolysis, or base hydrolysis. The organic and aqueous phases were analyzed by LSC and HPLC.

Total radioactivity in the soil was determined by LSC following combustion. The soil was refluxed sequentially once with hexane, once with acetonitrile, once with 10% aqueous acetonitrile, and once with 0.1 N hydrochloric acid:methanol. The aqueous acetonitrile and 0.1 N hydrochloric acid:methanol fractions were evaporated under vacuum, and the resulting residues were partitioned between water and chloroform. All fractions were analyzed for total radioactivity by LSC and analyzed by TLC or HPLC as described in the plant analysis section. Unextractable [^{14}C]residues in the soil were quantified by LSC following combustion.



ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

WALKER'S MILL, BARLEY MILL PLAZA

P.O. Box 60036

WILMINGTON, DELAWARE 19880-0038

AGRICULTURAL PRODUCTS DEPARTMENT

October 2, 1989

Mr. Robert J. Taylor
Product Manager (25)
Fungicide-Herbicide Branch
Registration Division (H7505C)
U.S. EPA
Crystal Mall Building #2
Arlington, VA 22202

SUBJECT: Submission of Additional Information for Metribuzin
Confined Rotational Crop Study
(Ref. letter R.J. Taylor to M.M. Chubb 4/13/89)

Dear Mr. Taylor:

Attached are three copies of the following:

Supplement to:
Metribuzin Confined Accumulation Study of Peanuts
Motupali V. Naidu
AMR 563-86
(MRID Accession No. 40577701)

We are providing additional information per the referenced letter to upgrade this study to be acceptable.

We appreciate your prompt review of this study.

Sincerely,

Marie M. Chubb
Registration & Regulatory Affairs

MMC/Iwl



United States Environmental Protection Agency
Office of Pesticide Programs (TS-767)
Washington, DC 20460

OPP Identifier Number

138207

Application for Pesticide: ☒ Registration ☐ Amendment

Section I

1. Company/Product Number... 352-390
2. Date... October 2, 1989
3. Product Manager... R. J. Taylor, PM 25
4. Proposed Classification... ☒ General ☐ Restricted

5. Name and Address of Applicant (Include ZIP Code)

E. I. Du Pont De Nemours & Company
Walker's Mill, Barley Mill Plaza
P. O. Box 80038
Wilmington, DE 19880-0038

☐ Check if this is a new address

6. Product Name

Du Pont Lexone® DF Herbicide

Section II - Amendment Information

1. Subject... ☒ Resubmission in response to Agency letter ☐ Final printed label in response to Agency letter ☒ Other (explain below) Date of Letter

To provide additional information for confined Rotational greenhouse study

Attachment: 3 copies of V.L.

Supplement to:

Metribuzin Confined Accumulation Study of Peanuts

M.V. Naidu

(AMR 563-86)

Reference letter M.M. Chubb to R.J. Taylor

Section III

1. Material This Product Will Be Packaged in... Child-Resistant Packaging ☐ Yes ☐ No Unit Packaging ☐ Yes ☐ No Water-Soluble Packaging ☐ Yes ☐ No
If "Yes," Unit package wgt No. per container Package weight No. per container
2. Type of Container... ☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specify)
3. Location of Net Contents Information... ☐ Label ☐ Container 4. Size(s) of Retail Container
5. Location of Label Directions... ☐ On Label ☐ On material accompanying product 6. Manner in Which Label Is Affixed To Product... ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other (Specify)

Section IV

1. Contact Point (Complete items directly below for identification of individual to be contacted, if necessary, to process this application).

Name

Marie M. Chubb

Title

Registration Specialist

Telephone No. (Include Area Code)

(302) 992-6278

6. Date Application Received (Stamp)

Certification
I certify that the statements I have made on this form and all attachments thereto are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature

Marie M. Chubb

3. Title

Registration Specialist

4. Typed Name

Marie M. Chubb

5. Date Signed

October 2, 1989



United States Environmental Protection Agency
Office of Pesticide Programs
Washington, DC 20460

Data Review Record

Confidential Business Information - Does not contain
National Security Information (E.O. 12065)

Pack Number

Date Received

50568
EFED

5-1-90

1. Product Name

Chemical Name

2. Identifying Number

3. Record Number

4. Action Code

5. MRID/ Accession Number

6. Study Guideline or Narrative

7. Reference No.

8. Date Rec'd (EPA)

9. Prod/Review Mgr/DCI

10. PM/RM Team No.

11. Date to HED/
EFED/RD/BEAD

12. Proj Return Date

13. Date Returned
to RD/SRRD

Instructions

Letter to A. Pictor
Information requested in review of 12/21/88
for review is copy of reply to DFB Referral

Ch Code 101101-4

This Section Applies to Review of Studies Only

14. Check Applicable Box

☐

Adverse 6(a)(2) Data (405)

☐

Generic Data (Reregistration)(660)

☐

Special Review Data (870)

☐

Product Specific Data (Reregistration)(655)

15. No. of Individual Studies
Submitted

16. Have any of the above studies (in whole or in part) been previously submitted for review?

☐

Yes (Please identify the study(ies))

☐

No

17. Related Actions

18.

To

Type of Review

19. Reviews Also Sent to

20. Data Review Criteria

HED

Science Analysis & Coordination
Toxicology/HFA
Toxicology/IR
Dietary Exposure
Nondietary Exposure

SAC
TOX/HFA
TOX/IR
DEB
NDE

PC
PL
EA
AC
BA

A. Policy Note No. 31

1 = data which meet 6(a)(2) or
meet 3(c)(2)(B) flagging
criteria

2 = data of particular concern
from registration standard

3 = data necessary to determine
tiered testing requirements

B. Section 18

1 = data in support of section 3
in lieu of section 18

C. Inert Ingredients

1 = data in support of continued
use of List 1 inert

EFED

Ecological Effects
Environmental Fate & Groundwater

EEB
EFGWB

SRRD

Special Review
Reregistration
Generic Chemical Support

SR
RER
GSC

RD

Insecticide-Rodenticide
Fungicide-Herbicide
Antimicrobial
Product Chemistry
Precautionary Labeling

IR
FH
AM

BEAD

Economic Analysis
Analytical Chemistry
Biological Analysis

☐ Confidential Statement of Formula
(EPA Form 8570-4) Attached (Trade Secrets)

☐ Label Attached